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Zheng, Hua; Hébert, Harry L.; Chatziperi, Athanasia; Meng, Weihua; Smith, Blair H.; Yan, Jing

Published in:
British Journal of Anaesthesia

DOI:
10.1016/j.bja.2020.08.049

Publication date:
2020

BJA
British Journal of Anaesthesia

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Journal:	*British Journal of Anaesthesia*
Manuscript ID	BJA-2020-01499-HH930.R2
Article Type:	Review article
Date Submitted by the Author:	n/a
Complete List of Authors:	Zheng, Hua; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Anesthesiology and Pain Medicine Hebert, Harry ; University of Dundee, Division of Population Health and Genomics Chatziperi, Athanasia; Western General Hospital, Department of Anaesthesia and Pain Medicine meng, weihua; University of Dundee, Division of Population Health and Genomics Smith, Blair; University of Dundee, Division of Population Health Sciences Yan, Jing; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Anesthesiology and Pain Medicine Zhou, Zhiqiang; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Anesthesiology and Pain Medicine Zhang, Xianwei; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Anesthesiology and Pain Medicine Luo, Ailin; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Anesthesiology and Pain Medicine Wang, Liuming; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Medical Affairs Office Zhu, Wentao; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Orthopedics Hu, Junbo; Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Department of Gastrointestinal Surgery Center Colvin, Lesley; University of Dundee, Division of Population Health Sciences
Keywords:	Coronavirus, COVID-19, SARS-CoV-2, perioperative, caesarean section, rapid review

Perioperative management of patients with suspected or confirmed COVID-19. Recommendations based on a rapid review and retrospective cohort study of outcomes in Tongji Hospital, Wuhan.

Short title: COVID-19 perioperative management

Hua Zheng[1†], Harry L. Hébert[2†], Athanasia Chatziperi[3], Weihua Meng[2], Blair H. Smith[2], Jing Yan[1], Zhiqiang Zhou[1], Xianwei Zhang[1], Ailin Luo[1], Liuming Wang[4], Wentao Zhu[5], Junbo Hu[6*], Lesley A. Colvin[2*]

1. Department of Anesthesiology and Pain Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China
2. Division of Population Health and Genomics, School of Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee DD2 4BF, Scotland, UK
3. Department of Anaesthesia and Pain Medicine, Western General Hospital, NHS Lothian, Edinburgh, UK
4. Medical Affairs Office, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China
5. Department of Orthopedics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China
6. Department of Gastrointestinal Surgery Center, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

[†]These authors contributed equally to this work

*Corresponding authors. E-mails: jbhu@tjh.tjmu.edu.cn, l.a.colvin@dundee.ac.uk

Abstract

Background: Current guidelines for perioperative management of COVID-19 are mainly based on extrapolated evidence or expert opinion. We aimed to systematically investigate how COVID-19 affects perioperative management and clinical outcomes, to develop evidence-base guidelines.

Methods: First, we conducted a rapid literature review in Embase, Medline, PubMed, Scopus, and Web of Science (1st January to 1st July 2020), using a predefined protocol. Secondly, we performed a retrospective cohort analysis of 166 women undergoing Caesarean section at Tongji Hospital, Wuhan during the COVID-19 pandemic. Demographic, imaging, laboratory, and clinical data were obtained from electronic medical records.

Results: The review identified 26 studies, mainly case reports/series. One large cohort reported greater mortality in elective surgery patients diagnosed after, rather than before surgery. Higher 30-day mortality was associated with emergency surgery, major surgery, poorer preoperative condition and surgery for malignancy. Regional anaesthesia was favoured in most studies and personal protective equipment (PPE) was generally used by healthcare workers (HCW), but its use was poorly described for patients. In the retrospective cohort study, duration of surgery, oxygen therapy and hospital stay were longer in suspected or confirmed patients than negative patients, but there were no differences in neonatal outcomes. None of the 262 participating HCWs was infected with SARS-CoV-2 when using level 3 PPE perioperatively.

Conclusions: When COVID-19 is suspected, testing should be considered before non-urgent surgery. Until further evidence is available, HCWs should use level 3 PPE perioperatively for suspected or confirmed patients, but research is needed on its timing and specifications. Further research must examine longer-term outcomes.

Registration: The rapid review was registered in PROSPERO (ID: CRD42020182891).

Keywords: Coronavirus, COVID-19, SARS-CoV-2, perioperative, Caesarean section, rapid review

Introduction

Coronavirus disease 2019 (COVID-19), resulting from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has become a global pandemic since it was first described in Wuhan, China in December 2019[1], and was declared a public health emergency. As of 10th August 2020, over 19 million cases and over 728,000 deaths have been reported worldwide[2]. In the UK alone, 310,829 cases have been reported with 46,574 deaths, and in China there have been 89,270 cases and 4,693 deaths[2]. In response to this health crisis, guidelines have been published on the clinical management of patients undergoing surgery to prevent transmission to healthcare workers (HCW) and adverse outcomes in patients[3, 4]. However these are mainly based on pre-existing practices rather than on data from patients with suspected or confirmed COVID-19, and little is known about how perioperative techniques affect transmission rates and outcomes in patients with COVID-19. Furthermore, a rapid review of clinical guidelines published early in the COVID-19 pandemic concluded that their overall quality was low and their focus should be on evidence-based recommendations, rather than consensus[5]. This study therefore had 2 objectives:

I. To conduct a rapid review of studies and case reports examining the management of patients with suspected or confirmed COVID-19 undergoing surgery, and subsequent morbidity, mortality, length of hospital stay, use of intensive care, respiratory and pain support, and COVID-19 transmission to HCWs.

II. To examine perioperative approaches and outcomes in a series of Caesarean section operations undertaken in Tongji Hospital, Wuhan, during the COVID-19 outbreak

Methods

I. Rapid Review

The reporting of this review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[6]. Due to the fast-evolving nature of COVID-19 and the need to produce clinical evidence for making recommendations on patient care that are readily available to HCWs in a timely manner, we chose to adopt a rapid approach to the review[7]. This involved a streamlined protocol whereby article identification, appraisal and data extraction were shared between two reviewers, with some overlap for quality control, instead of complete independent duplication. Details of the protocol were registered on PROSPERO: International prospective register of systematic reviews (ID: CRD42020182891) and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=182891.

Eligibility Criteria

Population: Any patient undergoing surgery who had confirmed or suspected COVID-19 at the time of surgery.

Intervention: Any form of surgery and perioperative management undertaken whilst the participant was suspected or confirmed as having COVID-19, except where the procedure was conducted to treat COVID-19. Any studies not reporting details of patient management at any time during the perioperative period (defined as 24 hours before and after surgery) were excluded from the review. Studies were also excluded if they included patients who did not undergo surgery, and where it was not possible to identify them separately from surgical patients.

Comparator: Where relevant, patients with suspected or confirmed COVID-19 who were not subject to perioperative interventions.

Outcomes: Patient, HCW and neonatal postoperative outcomes, where relevant.

Study type: Observational studies including cross-sectional, case-control and cohort designs as well as case-series or case-reports and randomized control trials (RCTs) could be included. As the database search, article screening and data extraction

processes were conducted by UK-based authors, only English language articles were considered, to avoid misinterpretation of the data. Unpublished studies, conference abstracts and research theses or dissertations were also excluded (Table 1).

We searched PubMed, MEDLINE, EMBASE, Scopus, and Web of Science for original articles, reported in English. Databases were searched from 1st January 2020, with initial search to 4th May 2020; the search was updated on 1st July 2020. As the purpose of this study is to provide both clinical evidence and recommendations for further research in a timely manner, it was decided to exclude studies with a sample size of less than 15 in the rerun of search terms (4th May-1st July 2020). Such studies are likely to be dominated by lower quality case reports, which would not contribute substantially to the overall evidence presented in this study. In addition the reference sections of included studies were also checked for relevant studies.

The search terms used for all 5 databases included words related to COVID-19 (the population), surgical interventions and perioperative management (the interventions). Comparator, outcomes and study type search terms were not used. Where available, the study year filter was set to 2020 (Supplementary Table S1).

After retrieving articles from the databases, non-English language and duplicates were removed. HLH and LAC then independently screened the titles and abstracts according to the inclusion and exclusion criteria to identify relevant studies. Remaining articles then went through full-text review (HLH and LAC), noting reasons for all exclusions. Any differences in opinion were settled by discussion between the reviewers and, where necessary, the wider research team.

Data Extraction

A pro forma spreadsheet was constructed and data extraction was conducted independently by HLH and AC, who reviewed an equal number of studies with a 6-study overlap for quality control. Any differences in data extraction for the overlapped studies were resolved between HLH and AC. Due to the rapid nature of the review, study authors were not contacted to resolve missing data or identify

further studies.

The following data items were extracted:

1. Study details – authors, journal of publication, date of publication, country/countries where the study took place, sample size and study design.
2. Patient characteristics – age, gender, body mass index (BMI)/weight, comorbidities and method of diagnosing or suspecting COVID-19.
3. Surgical details – type, schedule, indications, duration and other relevant details.
4. Perioperative management – HCW use and level of personal protective equipment (PPE), patient use of PPE, patient time between symptoms and surgery, type of anaesthesia (e.g. general/regional), analgesics used, pain assessment, vasopressors used, blood loss and any other relevant details.
5. Postoperative outcomes – HCW COVID-19 status, patient discharge status, length of hospital stay, use of intensive care unit (ICU) or high dependency unit (HDU), level of respiratory support, use of analgesia, mortality and, where relevant to the study, neonatal COVID-19 status, Apgar score, mortality, discharge status and any other relevant reported details

Risk of Bias (Quality) Assessment

The quality of reporting of all included studies was evaluated by HLH and AC according to the CAse REport (CARE) guidelines[8] for case reports/series or the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[9] for cross-sectional, case-control and cohort studies. A quality score[10, 11] was calculated for each article based on a checklist of 36 items for CARE (Supplementary Table S2) and 32-34 items for STROBE (Supplementary Table S3), depending on the type of observational study. The presence of an item scored one, absence scored zero and the total was calculated. A percentage of the maximum possible score was also calculated and “high quality” was defined as any study achieving a score of 80% or greater[10, 12]. “Low quality” was defined as any study with

a score of less than 80%. Higher scores indicate studies with reporting of higher quality. Disagreements were resolved via discussion between the 2 reviewers.

Summary Measures

For case reports and series with sample size ≤5, numeric values are reported individually. Otherwise summary statistics are presented (e.g. median, mean, range, interquartile range [IQR] or standard deviation [SD]) as reported in original papers. Qualitative variables are reported as counts. A synthesis of the extracted data was constructed, structured around the type of surgery performed, surgical practices, population demographic and clinical characteristics, and type of outcome. Recommendations for the perioperative management of patients with COVID-19 were developed from the synthesised evidence, and tables were constructed to aid the presentation of the extracted data and quality assessment of each article.

II. Cohort Study

Study design and data sources and ethics

This single-centre, retrospective study was approved by the Institutional Review Board of Tongji hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB20200421). The requirement for informed consent from participants was waived under the regulations of the Institutional Review Board. Data, including demographic, clinical, imaging, laboratory, perioperative management, and maternal and fetal outcomes, were extracted from the electronic database of medical records at Tongji Hospital, and anonymised for analyses.

Data from all parturients who underwent Caesarean section (including emergency surgery) during the COVID-19 pandemic in Wuhan were included in this study. In order to ensure completeness of reported data, we included all patients who had undergone Caesarean section in the defined time period. Part of this data has been reported previously by other groups [13, 14]. COVID-19 case definitions were based on

the National Health Commission of China's diagnostic criteria (seventh edition) (Box 1)[15]. A confirmed case of COVID-19 was defined as a suspected case with a positive result of real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of respiratory tract specimens or serum-specific antibodies to SARS-CoV-2. If the results of 2 RT-PCR tests taken at least 24-hour apart, and serum-specific antibodies to SARS-CoV-2 detected at least 7 days after the onset of the disease, were negative in a suspected case, the diagnosis of COVID-19 was excluded. All patients were tested with RT-PCR or antibodies or CT when possible. If COVID-19 was suspected or confirmed, follow-up tests were performed after surgery.

Perioperative management

Before entering the operating room, triage was performed by obstetricians and anaesthetists, including medical history review, brief physical examination, and reviewing blood test results, chest computed tomography (CT), test for nucleic acid of SARS-CoV-2 or SARS-CoV-2 antibodies. Because individuals might be infected with SARS-CoV-2 but be asymptomatic, all patients were placed in an isolation holding area and transferred to a dedicated negative pressure system operating room with an anteroom beside it (buffer area). The patients wore surgical or N95 masks throughout the process. After the patient entered the operating room, routine monitoring including continuous electrocardiograph, regular non-invasive blood pressure, and peripheral pulse oximetry were performed. Spinal anaesthesia or combined spinal epidural anaesthesia was the primary choice. General anaesthesia with tracheal intubation was an option under certain circumstances such as contraindications of spinal anaesthesia, maternal or fetal emergencies, or failed spinal anaesthesia. During the intubation, surgeons and nurses remained in the operating room, to ensure that surgery started as soon as possible after induction. The neonatal team was notified before delivery, in order to attend and make any necessary preparations. After delivery, the newborns were cleaned immediately to remove blood clots, meconium and amniotic fluid. The newborns were then placed

under a radiant warmer in a cordoned-off area in the operating room. The Apgar scores of newborns were assessed at 1 and 5 minutes. For patients with suspected or confirmed COVID-19, their newborns were transferred to a neonatology isolation room shortly after delivery. SARS-CoV-2 nucleic acid tests were then carried out as soon as possible in all newborns. Maternal contact was not allowed. One day after surgery, full blood count and coagulation tests were performed in parturients. If COVID-19 was suspected or confirmed, chest CT, nucleic acid of SARS-CoV-2 or SARS-CoV-2 antibodies were tested again. Body temperatures or any other symptoms associated with COVID-19 were recorded daily by nurses, throughout the hospital stay. According to the parturients' clinical condition, supplemental oxygen was delivered via nasal cannula or mask to maintain an SpO2 of 95% and above. Other methods of non-invasive or invasive ventilation were considered if necessary. Diclofenac and/or dezocine was given, as requested by the parturients, to relieve postoperative pain.

Perioperative protection and postoperative evaluation of healthcare workers

Self-protection precautions were strictly followed by all participating HCWs. Level 3 PPE including N95 mask, fluid-resistant gown, goggle, face shield, disposable hair cover, head covering, 2 layers of gloves, and fluid-resistant shoe covers, was used by all HCWs involved. PPE was donned before entering the operating room and was doffed after exiting operating room in buffer area. All HCWs involved had a 24-hour duty shift every one to two weeks. They were required to report any COVID-19 related symptoms such as fever, cough or fatigue. At the beginning of April, 2020, all HCWs were required to have a SARS-CoV-2 antibodies detection test, a test for nucleic acid of SARS-CoV-2 on nasopharyngeal swabs and a chest CT scan.

Statistical analysis

Suspected or confirmed cases were categorised together and compared with negative cases. Maternal outcomes including duration of operation, oxygen therapy

and hospital stay, and fetal outcomes such as Apgar scores at 1 minute and 5 minutes were compared between groups. Continuous variables are presented as median (IQR). These data failed the Shapiro-Wilk test for normality and significance was calculated using Mann-Whitney U tests. Categorical variables are expressed as number (%) and analysed using chi-square tests. SPSS 21.0 statistical software (SPSS, Inc. Chicago, IL, USA) was used for all statistical analyses. A 2-sided P-value <0.05 was considered to be statistically significant.

Results

I. Rapid Review

Study Selection

The workflow for identifying and screening articles is provided in figure 1. The initial literature searches yielded 3,227 papers. The re-run of the search yielded a further 107 articles. After removal of duplicates, non-English language papers and title and abstract screening, 64 articles remained for full-text review. Articles identified during the re-run of search terms (from 4th May to 1st July, 2020) that were excluded on the basis of having a sample size ≤15 are shown in Supplementary Table S4. A full list of the 38 articles excluded on full-text review, with reasons, is provided in Supplementary Table S5. We therefore identified 26 articles for inclusion in this review[16-41].

Study Characteristics

The characteristics of each included study are summarized in Table 2. There were no RCTs. Twenty-two of the papers were lower quality case reports or case series[16, 17, 19, 21-32, 34-39, 41]. The remaining 4 were observational studies, of which 2 were cohort studies[20, 33], 1 was a small cross-sectional study (n=7)[18] and 1 was a retrospective 4-centre clinical study (n=37)[40]. The cross-sectional study was published without peer-review[18]. Only one study met our definition of "high quality"[33].

Sixteen of the studies were conducted in China, where the virus was first reported[19, 21, 22, 25, 27, 29, 30, 32, 34-41]. Three were conducted in Italy[18], whilst 1 study was conducted in each of Iran[18], Peru[16], Portugal[31], Republic of Korea[28], Sweden[26] and USA[24]. One paper was a multi-centre cohort study conducted in 24 different countries, led by a centre in the UK[33].

Risk of Bias (Quality) Assessment

CARE Quality assessment scores ranged from 7 to 26 (out of 36) for the case reports

and case series STROBE scores ranged from 10 to 33 (out of 34) for the observational studies (Table 2). A full breakdown of scores for each study is provided in Supplementary Tables S6 and S7.

Due to the limited sample sizes of the included studies, the heterogeneity in surgeries performed and approaches to perioperative management, and the inherent lack of comparative groups in the case reports, it was not possible to conduct a meta-analysis to estimate effect sizes and we could not quantitatively assess risk of bias across studies.

COVID-19 status

Diagnosis of COVID-19, and timing of diagnosis (relative to surgical procedure) were variably reported, applying a range of diagnostic criteria. Suspected COVID-19 was usually based on relevant symptoms. All of the studies used RT-PCR for SARS-CoV-2 RNA or chest CT scans for diagnosis (though 1 study did not report diagnostic criteria[32]). Four studies used RT-PCR only[26, 29, 31, 35], 2 studies used CT scans[18, 27] only and 19 studies used a combination of both[16, 17, 19-25, 28, 30, 33-41]. In some places RT-PCR was not available[33]. Specimens used for RT-PCR included nasopharyngeal, oropharyngeal, sputum, tracheal tube tip and bronchoalveolar lavage. Although not fully reported in all studies, RT-PCR tests were negative in some cases despite CT findings (and in some cases, symptoms) being indicative of COVID-19[25, 41].

Perioperative management

The total number of surgical procedures reported in the included studies was 1,370, including gastrointestinal/abdominal (n=393)[18, 20, 25, 33, 40], orthopaedic (n=352)[17, 18, 20, 33, 40, 41], obstetric/gynaecological (n=166)[16, 19, 21-23, 26, 28-31, 33-41], cardiothoracic/vascular (n=146)[20, 24, 27, 33, 40], hepatobiliary (n=62)[33], neurosurgical (n=47)[20, 33, 40], head and neck (n=40)[33], urological (n=37)[33], other surgeries (n=63)[33, 40] and missing details (n=64)[32, 33]. The schedule of the surgeries, where reported, were classed as elective (n=316), and urgent, or emergency (n=949). At least 153/166 of

the obstetric/gynaecological surgeries were Caesarean sections. Most of the other surgeries were for cancer or trauma (Supplementary Table S8).

Most studies reported surgical procedures performed under neuraxial anaesthesia (Table 3). Ten reported procedures (53 Caesarean sections, 17 orthopaedic) using neuraxial anaesthesia only[17, 22, 26, 28, 30, 31, 34, 36, 37, 41] and 3 reported procedures (5 aortic dissections and 1 Caesarean section) using general anaesthesia only[16, 24, 27], whilst 6 reported a mix of surgeries performed using either general or neuraxial anaesthesia[19, 20, 32, 33, 35, 40]. When reported, spinal, epidural or a combination of the 2 methods were used. Exact details of which anaesthetics and analgesics were used were only reported in 5 of the 26 studies[19, 28, 34, 37, 41]. It is not clear whether there were any changes from standard anaesthetic/analgesic practice because of COVID-19.

Use of Personal Protective Equipment (PPE) and infection reduction strategies

Patient use of PPE was poorly reported, with only 9 studies stating that patients wore any protection[19, 21-23, 28, 29, 35, 38, 39]. Six of these reported the use of surgical masks only[19, 21, 22, 28, 35, 38], with N95 masks being more specifically mentioned in 3 studies[21, 22, 28].

HCW use of PPE was more comprehensively reported, with 16 studies describing its perioperative use[19, 22-31, 35-38, 41]. The reported type of PPE used by HCWs was wide-ranging with N95 mask, disposable surgical cap, medical goggles or positive-pressure headgear, and disposable protective clothing, gloves and shoes/shoe covers described. However, details on duration of PPE use, and at what points during the perioperative period (e.g. only during intubation/aerosol generating procedures) were lacking.

Nine of the studies in our review reported using operating rooms with negative pressure[19, 21, 22, 24, 28, 29, 35, 36, 38]. Only 1 of these studies also described the postoperative care of a patient in a negative pressure ICU[24], although 2 studies described sending neonates to negative-pressure wards immediately after birth[29, 31].

However details on other elements of ventilation such as air changes per hour, direction and filtration were lacking.

Twelve of the studies describing Caesarean sections reported immediate separation of the neonates from their mothers following delivery, aiming to reduce risks of postpartum infection. Eight of these were conducted in China[19, 21, 30, 34-36, 38, 39], while the other 4 were conducted in Italy[23], Portugal[31], Peru[16], and the Republic of Korea[28]. Three studies reported on the decontamination of the anaesthesia machine following surgery[19, 24, 40], with two of the studies reporting no HCW infection with COVID-19[19, 24] (the third study did not report HCW COVID-19 status[40]). A further study reported the discarding of disposable anaesthetic devices after single use[27].

Patient outcomes

Patient outcomes reported included length of hospital stay, requirement for critical care, level of respiratory support and respiratory complications, discharge status, and mortality (Supplementary Table S9). None of the included studies reported on all these outcomes. Reporting on discharge status was very limited. Twelve studies reported length of stay in hospital, which ranged from 5 to 52 days[18-20, 22, 25, 26, 28-31, 33, 35].

In the largest cohort study (n=1,128), the median length of stay in hospital (IQR) was 10 days (3-27) for minor surgery and 17 days (8-29) for major surgery, reported in a total of 1,083 patients[33]. This study reported an overall 30-day mortality of 23.8%, with a higher rate of mortality in patients undergoing elective surgery where the presence of SARS-CoV-2 virus had been confirmed postoperatively rather than preoperatively (20.4% vs 9.1%). A number of patient factors were found to be associated with higher 30-day mortality including male sex (odds ratio [OR] = 1.75, 95% confidence interval [CI] = 1.28-1.40), emergency surgery (OR = 1.67, 95% CI = 1.06-2.63), major surgery (OR = 1.52, 95% CI = 1.01-2.31), older age (>70 years) (OR = 2.30, 95% CI = 1.65-3.22), poorer preoperative condition as assessed by American Society of Anesthesiologists' physical status classification (OR = 2.35, 95% CI =

1.57-3.53) and undergoing surgery for malignancy (OR = 1.55, 95% CI = 1.01-2.39). Pulmonary complications, defined as pneumonia, acute respiratory distress syndrome or unexpected postoperative ventilation, occurred in 51.2% of patients with COVID-19, and was associated with increased mortality compared to those who did not develop complications (38.0% vs 8.7%).

Postoperative use of ICU was poorly reported and where it was reported (9 studies)[18, 20, 22-25, 27, 32, 33], it was not always clear whether the patients had been transferred there due to COVID-19, or whether they would have been transferred there anyway because of the indication for surgery[27]. Postoperative respiratory support was described in 10 studies[17, 18, 20, 23, 24, 26, 27, 31, 33, 37], but as with ICU use it was not clear in some papers whether this would have occurred anyway. Postoperative use of analgesia was only reported in 3 studies[17, 28, 37], with only 1 reporting any formal pain assessment[19].

Reporting of outcomes in neonates was more consistent, with 16 studies (out of 19 studies involving obstetric surgeries) reporting COVID-19 status[16, 19, 21-23, 26, 28-31, 34-39] and 12 of those studies reporting only negative test results, mainly for RT-PCR[19, 21, 22, 26, 28-31, 34-38]. Of the other 4 studies, 2 reported only positive tests[23, 39] and 2 reported a mix of positive and negative results[16, 35]. Apgar scores were reported in 14 studies (of the 19 involving obstetric surgeries), and these were generally very good or excellent[16, 19, 21-23, 26, 28, 30, 31, 34-38]. No neonatal mortalities were reported in any of the studies.

Healthcare worker outcomes

Most of the studies reported outcomes within a few days to 2 weeks after surgery.

HCW COVID-19 outcomes were only reported in 10 studies[19, 22-24, 28, 30, 32, 35, 37, 41]. One of these, a case series of 49 patients including outcomes from 44 anaesthetists, reported 5 anaesthetists testing positive for SARS-CoV-2 on RT-PCR testing, following delivery of spinal anaesthesia during Caesarean section or orthopaedic surgery[41]. One of the 5 anaesthetists testing positive for SARS-CoV-2 had worn level 3 PPE (2.7%

of all who wore level 3 PPE), while 4 of them had worn level 1 PPE (57.1% of all who wore level 1 PPE), suggesting better HCW protection with level 3 PPE. This also appears to be supported by 8 of the other 9 studies where no HCW SARS-CoV-2 infections were reported when using PPE[19, 22-24, 28, 30, 35, 37]. Three of these studies reported level 3 PPE[22, 30, 37], 1 reported biosafety level 3[19] and 4 studies described PPE in detail including N95 mask, eye goggles, face shield and surgical gown[23, 24, 28, 35]. However we can only make tentative recommendations on the use of PPE as it was not clearly reported how long the PPE was worn before, during and/or after the surgery and whether any changes were made to the level of PPE worn at any stage (for example following intubation/extubation of the patient). Furthermore, we cannot be sure that HCW infection occurred as a result of caring for patients with COVID-19 rather than other sources such as infected colleagues or in the wider community[41].

II. Cohort Study

Patient characteristics

Between 23rd January 2020 and 31st March 2020, 166 parturients underwent Caesarean section and were included in this study. Before surgery, 2 patients were confirmed to be infected with SARS-CoV-2 and 36 patients were considered as suspected cases based on the above criteria (Box 1). After surgery, 5 suspected cases were confirmed and 11 suspected cases were ruled out. Finally, 7 confirmed cases and 20 suspected cases of COVID-19 were identified. One case report[14] and 5 patients (patient 1, 4, 5, 6 and 7) from a case series[13] were reported previously by others. The other 2 patients (patient 2 and 3) in the case series[13] undergoing caesarean section between 1st January, 2020 and 23rd January, 2020 were not included in the current study. All 20 suspected cases had imaging features of COVID-19. They were tested with RT-PCR only before discharge and the results were negative. For analysis, we combined these suspected cases and confirmed cases as 1 group (n=27) and patients not (suspected to be) infected with COVID-19 as a second

'negative' group (n=139). As shown in Supplementary Table 10, the BMI of suspected or confirmed patients was higher than that of negative patients (P = 0.034). Symptoms associated with COVID-19 occurred only in suspected or confirmed patients; fever was the commonest with an incidence of 44.4%, followed by cough (14.8%) and diarrhoea (3.7%).

Laboratory findings of patients before and after Caesarean section are summarised in Supplementary Table 11. Compared with baseline pre-procedural values, increased leukocyte and neutrophil counts were observed after surgery in all patients. Compared with negative patients, suspected or confirmed patients had lower leukocyte (P = 0.003 before surgery; P = 0.047 after surgery) and lymphocyte (P = 0.030 before surgery; P = 0.041 after surgery) counts during the perioperative period. Baseline preprocedural C-reactive protein levels in confirmed or suspected patients were higher than negative patients (P = 0.014), but were not difference from postsurgical levels. In negative patients, there were significantly elevated levels of CRP (P = 0.006) and D-dimer (P = 0.011) after surgery compared with baseline preprocedural values.

Characteristics of anaesthesia and surgery

An overview of parturients' intraoperative characteristics is shown in Supplementary Table 10. Regional anaesthesia was the commonest type of anaesthesia and was performed in 142 (85.5%). Duration of operation in suspected or confirmed patients was longer than that in negative patients (P = 0.003). However, there were no significant differences in blood loss, fluid management, or use of vasoactive drugs and flurbiprofen.

Maternal and fetal outcomes

As listed in Supplementary Table 10, 48.8% of patients received diclofenac and/or dezocine for postoperative pain. There was no significant difference between suspected or confirmed patients and negative patients. Both the duration of oxygen

therapy (P < 0.001) and length of hospital stay (P < 0.001) were significantly longer in suspected or confirmed patients than negative patients. No suspected or confirmed patients developed severe pneumonia or received non-invasive or invasive mechanical ventilation. However, a negative patient with liver cancer was intubated and died due to pulmonary embolism after surgery.

The medians of Apgar scores were 8 at 1 minute and 9 at 5 minutes. There were no apparent differences in the neonates when comparing the suspected or confirmed group with the negative group. In the negative group, a neonate delivered at 25 weeks' gestation died 10 min after birth. In the confirmed group, a neonatal COVID-19 infection with positive results of RT-PCR assay on pharyngeal swabs was reported 36 hours after birth, and this had been reported in a previous study[13]. However, the results of nucleic acid tests for SARS-CoV-2 on placenta specimens, cord blood and mother's breast milk in this mother–neonate dyad were all negative.

Postoperative evaluation of healthcare workers

A total of 262 HCWs including 71 anaesthetists, 60 obstetricians and 131 nurses (circulating nurses, instrument nurses and neonatal nurses) were involved in these Caesarean sections. Level 3 PPE was used by all the HCWs during the operation. None of them reported COVID-19 related symptoms during the COVID-19 pandemic. As of 15th April, 2020, none of them has been infected with the SARS-CoV-2 according to the CT scan findings, RT-PCR testing and/or SARS-CoV-2 antibodies testing.

Discussion

Our rapid literature review identified 26 studies reporting perioperative management of patients with suspected or confirmed COVID-19. To our knowledge this is the most comprehensive such review to date. Most studies were low quality case reports/series with low sample size, and even amongst the observational studies, perioperative management was not necessarily the main focus of any quantitative analysis conducted[20, 33] and was poorly reported[18]. Thus, a cohort study of Caesarean sections, especially focusing on perioperative management and patients and HCW outcomes, was performed to augment the included evidence base.

All studies included in the review used either RT-PCR or CT scans to diagnose SARS-CoV-2/COVID-19. This approach appears to be supported by the fact that RT-PCR testing did not always produce positive results, despite the presence of relevant clinical symptoms and the elimination of other viruses or comorbidities that could potentially explain those symptoms. In our cohort study, only 5 out of 27 participants with suspected or confirmed COVID-19 were positive for SARS-CoV-2 by RT-PCR. The wider literature has also reported uncertainty in diagnostic performance of RT-PCR[42] and when compared to CT scans their sensitivity ranges from 50-81%[43-45]. The use of CT scans does need to be balanced against the extra risk of exposing patients to radiation, particularly for women undergoing Caesarean section whose fetus will also be exposed[46]. This is an area that requires further investigation, but consideration should be given to using both approaches in diagnosing COVID-19.

The timing of COVID-19 testing also needs to be considered since higher mortality was reported in patients undergoing elective surgery where the presence of SARS-CoV-2 virus has been confirmed postoperatively rather than preoperatively (20.4% vs 9.1%)[33]. Performing tests preoperatively will enable informed decisions about the postponement of surgeries to be made for patients who test positive and are thus at increased risk of postoperative complications. There may also be requirements to ensure appropriate levels of care, such as facilities or staffing, are

available for the postoperative period should complications arise. COVID-19 testing may also influence ICU admissions and transmission to HCWs[47-49]. This further suggests that testing for possible SARS-CoV-2 infection should take place before surgery, as supported by The American Society of Anesthesiologists and Anesthesia Patient Safety Foundation joint guidelines[50]. However this might be difficult for emergency surgery, therefore a standardised diagnosis and treatment protocol for emergency patients should be developed. This is already happening in some places and whilst pre-operative screening will potentially increase the time between admission and surgery, initial evidence suggests that this risk can be minimised to the point that it can be balanced against the potential risk of performing surgical procedures in COVID-19 patients[51]. Further research is needed to establish whether the testing pathway is of more clinical benefit than not having it. In patients with suspected or confirmed COVID-19, the COVID-19 status of newborns should also be taken into account where relevant, and testing should be performed as soon as possible after delivery to help prevent transmission to HCWs and to ensure risk to the newborn is minimised, with early recognition and management of symptoms.

Despite being included in perioperative anaesthesiology guidelines for HCWs in both America and China[3, 50], PPE use was poorly reported by studies in patients (9 studies)[19, 21-23, 28, 29, 35, 38, 39]. Current guidance in the UK is that anyone with suspected or confirmed COVID-19 should wear a surgical face mask in clinical areas, communal waiting areas and during transportation as long as this does not compromise their clinical care[52]. In tuberculosis patients, the use of surgical facemasks has been shown to confer a 56% decreased risk of transmission compared to those not wearing a mask[53]. Furthermore, a literature review of studies analysing the effectiveness of respiratory protection for healthcare workers against infectious diseases found that guidelines were consistent in recommending at least an N95 respirator for care of patients with tuberculosis[54]. Despite this, there is currently no evidence that patient use of face masks reduces risk of COVID-19 transmission to HCWs, despite these studies not reporting any HCW infections[19, 21-23, 28, 29, 35, 38, 39]. Better reporting was

observed relating to HCWs themselves. A recent study has demonstrated the effectiveness of HCWs wearing PPE in preventing COVID-19 infection and advocated its continued use in the absence of a vaccine[55]. In our cohort study, none of the 262 HCWs developed COVID-19, suggesting that both regional and general anaesthesia can be delivered safely to patients with COVID-19, when surgical or N95 masks are applied in patients and level 3 PPE is used by HCWs during the perioperative period. The use of aprons, sterile fluid resistant disposable gown, sterile gloves, fluid resistant surgical masks and eye protection is recommended in the UK for Caesarean sections[56]. However, high level PPE is difficult to work in. For this reason it is important that future studies report on the duration of PPE use, whether they were used at particular points in the surgical process as some procedures are considered particularly high risk of airborne transmission and what levels constitute safe use[57]. It is also important to establish when PPE use is not necessary, to prevent wastage. Until these questions are addressed, HCWs should continue to use level 3 PPE during the perioperative period for all untested, suspected or confirmed cases of COVID-19 during times of pandemic and local outbreak[55].

Although this was not analysed directly with respect to postoperative outcomes, we found that 9 of the studies reported conducting surgical procedures in negative pressure operating rooms[19, 21, 22, 24, 28, 29, 35, 36, 38]. Negative pressure rooms are commonly used in infection control and ensure that air continually flows into the room, rather than the surrounding area. However, most hospitals only have a limited number of negative pressure operating rooms and therefore have to adapt additional rooms for this purpose. As current recommendations on minimum environmental ventilation requirements are based on previous non-COVID-19 work, further analysis and reporting on ventilation characteristics is required[3].

We identified 12 studies reporting the separation of neonates from mothers following Caesarean section[16, 19, 21, 23, 28, 30, 31, 34-36, 38, 39]. In our cohort study, newborns of mothers with suspected or confirmed COVID-19 were also transferred to an isolated observation ward after birth. At least in China, where 9 of those studies were

conducted, this represents a significant change from standard practice where normally mother and child skin-to-skin contact is encouraged, with recognised neurobiological benefits for mother and neonate. Although a newborn whose mother was confirmed with COVID-19 tested positive 36 hours after birth in our cohort study, whether the case was a contact transmission or a vertical transmission remains to be confirmed. Since the remaining studies did not accurately report level of mother and child contact, it is not possible to determine whether separation decreases the risk of SARS-CoV-2 infection. Emerging data suggest that allowing neonates to room in with their mothers and breastfeed confers low risk of perinatal and vertical transmission when a face mask is worn and proper hygiene is observed[58]. Because of these clinical implications and the potential impact on maternal-neonate interaction, this area requires urgent investigation.

A large cohort study identified patient and surgical factors associated with 30-day mortality[33]. This multi-centre study is easily the largest study of postoperative outcomes in patients with COVID-19 and because of the size and quality of the analysis, it is the only study from which we can make strong conclusions[33]. Consequently, future studies should consider longer-term reporting of health outcomes.

Previous studies found low mortality rates (1%) and requirement for respiratory support (10%) amongst pregnant women with COVID-19, as well as low neonatal transmission (5%), which our study supported[59, 60]. However, the duration of operation, oxygen therapy and length of hospital stay were significantly longer in suspected or confirmed patients than negative patients. An optimal approach to perioperative management in COVID-19 patients including appropriate use of anaesthetics and analgesics needs to be determined in future studies.

Strengths and Limitations

A major strength of the rapid review approach is the ability to quickly synthesise relevant original articles and identify current perioperative practices that are

associated with favourable postoperative outcomes. This has already enabled us to make early clinical recommendations (Box 2) on the perioperative management of COVID-19 to the Scottish Government, via the Scottish Intercollegiate Guidelines Network (SIGN), which can be disseminated to policymakers and HCWs and inform future perioperative practice (Roberta James, SIGN Programme Lead, personal communication, 2020). Because COVID-19 is a new and developing disease, hospital departments are having to adapt quickly to ensure optimum care and they rely on quick and accurate clinical guidance on how to provide this. However, many hospitals are not set up to conduct rapid research involving data collection, particularly during a global pandemic, and consequently there are gaps in reporting that this review has identified. A possible solution to this is to implement electronic health (eHealth) recording of patient data to ensure automated availability of relevant items of interest.

Converse to the rapid synthesis of the current literature, the short period of time that COVID-19 has been in existence, relative to other infectious diseases, means that there has not been enough time for many large and comprehensive cohort studies to be published and therefore the majority of studies included in this review are case reports and series. This means that the clinical implications of these studies should be treated with caution until further robust studies are published, preferably in the form of RCTs such as the Randomised Evaluation Of COVID-19 Therapy (RECOVERY) Trial (https://www.recoverytrial.net/)[61].

The rapid nature of this review means that more recently published articles may have been missed, though we mitigated this risk by conducting a further (targeted) literature search prior to submission. Excluding those not in English is pertinent given the global status of the COVID-19 pandemic. We also had to exclude 2 studies from Tongji Hospital in Wuhan as some of the participants were also included in the cohort study for this paper[13, 14].

Conclusions

From this rapid literature review and cohort study, we can make early clinical and research recommendations around the perioperative management of patients with suspected or confirmed COVID-19. These are presented in Box 2 and include timing of COVID-19 testing prior to surgery, more detailed reporting of patients' and HCWs' use of PPE, more detailed reporting of the perioperative use of anaesthesia and analgesia, and research into the longer term consequences of COVID-19. Together it is anticipated that these recommendations will contribute to improved postoperative outcomes for both patients with COVID-19 and HCWs treating those patients.

Details of Author Contributions

Study conception and design: HZ, WM, BHS, JH and LAC

Data acquisition: HZ, JY, ZZ, XZ, AL, LW, WZ, HLH and AC

Data analysis and interpretation: all authors

Drafting the article and revising for important intellectual content: all authors

Final approval of the published version: all authors.

Acknowledgements

We thank Lin Yan and Gang Chen from Department of Anesthesiology and Pain Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, for their efforts in collecting the information that was used in this study; and all the patients and healthcare workers involved in the study.

Declaration of Interests

The authors declare that they have no conflict of interest.

Funding

This work was partly supported by the University of Dundee Global Challenges Research Fund.

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Figure 1 - PRISMA flow diagram for the identification and screening of articles for inclusion in the review

Table 1 – Inclusion and exclusion criteria for studies in the review

Inclusion Criteria	Exclusion Criteria
1. Patients with confirmed or suspected COVID-19 who have undergone surgery or healthcare workers who have treated surgical patients with confirmed or suspected COVID-19	1. Unpublished studies, conference abstracts and research theses or dissertations
2. Observational studies including case reports, case series, case-control, cross-sectional, cohort and randomised control trials.	2. Studies that do not provide any perioperative management details (defined as the time from when the decision to operate was made to 24 hours after surgery).
3. Written in English	3. Studies where the patients are not suspected of or confirmed as having COVID-19 during surgery
	4. Studies that do not report patients that have undergone surgery separately from those that have not undergone surgery.
	5. Studies reporting surgery only conducted to treat COVID-19
	6. Studies[13, 14] that included participants that have also been included in the cohort study of this paper

COVID-19, Coronavirus disease 2019

Table 2 – Characteristics and quality assessment of the studies included in this review

Authors	Date of Publication	Country	Study Design	Surgery	Method of Suspecting/Diagnosing COVID-19 in Patient(s)	Sample Size	STROBE/CARE score (%)*
Alzamora *et al.*[16]	18/04/2020	Peru	Case report	Caesarean section	Nasopharyngeal RT-PCR, CT scan	1	22 (61%)
Catellani *et al.*[17]	30/04/2020	Italy	Case series	Orthopaedic	Oropharyngeal RT-PCR, thoracic CT scan	16 (13 underwent surgery)	21 (58%)
Chehrassan *et al.*[18]	14/04/2020	Iran	Cross-sectional	5 Orthopaedic, 1 abdominal	High resolution CT scan	7 (6 underwent surgery)	12 (37%)
Chen *et al.*[19]	16/03/2020	China	Case series	Caesarean section	Nasal RT-PCR, chest CT Scan	17	22 (61%)
Doglietto *et al.*[20]	12/06/2020	Italy	Cohort	22 Orthopaedic, 7 vascular, 6 neurological, 5 general, 1 thoracic	Nasopharyngeal RT-PCR, chest CT scan, chest radiography	41	26 (76%)
Dong *et al.*[21]	26/03/2020	China	Case report	Caesarean section	Nasopharyngeal RT-PCR, chest CT scan	1	18 (50%)
Du *et al.*[22]	19/05/2020	China	Case report	Caesarean section	Pharyngeal RT-PCR, CT scan	1	18 (50%)
Ferrazzi *et*	27/04/2020	Italy	Case series	Caesarean section	Throat swab RT-PCR	42 (18	19 (52%)

al.[23]					(confirmative chest X-ray)	underwent surgery)	
Firstenberg *et al*.[24]	19/04/2020	USA	Case report	Cardiothoracic	CT scan (preoperatively), RT-PCT (postoperatively, not explicitly stated)	1	25 (69%)
Gao *et al*.[25]	18/04/2020	China	Case series	Abdominal	Chest CT scan and radiography (preoperatively), oropharyngeal RT-PCR (postoperatively)	4	17 (47%)
Gidlöf *et al*.[26]	06/04/2020	Sweden	Case report	Caesarean section	Nasopharyngeal RNA test	1	15 (41%)
He *et al*.[27]	21/03/2020	China	Case series	Cardiothoracic	CT scan and clinical symptoms	4	13 (36%)
Lee *et al*.[28]	31/03/2020	Republic of Korea	Case report	Caesarean section	Sputum and nasopharyngeal RT-PCR, chest CT-Scan and chest radiography	1	21 (58%)
Li *et al*.[29]	2020, exact data unclear	China	Case report	Caesarean section	RT-PCR (not explicitly stated) of sputum sample	1	20 (55%)
Lu *et al*.[30]	24/04/2020	China	Case report	Caesarean section	Throat swab RT-PCR, chest CT-scan	1	24 (66%)
Lyra *et al*.[31]	20/04/2020	Portugal	Case report	Caesarean section	Nasopharyngeal and oropharyngeal RT-PCR	1	18 (50%)
Mi *et al*.[32]	09/06/2020	China	Case series	Not reported	Not reported	28	7 (19%)

Nepogodiev *et al.*[33]	29/05/2020	24 countries (led by UK)	Cohort	373 gastrointestinal and general, 302 orthopaedic, 86 cardiothoracic, 62 hepatobiliary, 51 obstetric, 45 vascular, 40 head and neck, 39 neurosurgery, 37 urological, 57 other and 36 missing	Nasal swab or bronchoalveolar lavage RT-PCR, relevant clinical symptoms (including cough, fever or myalgia), or radiological findings (thorax CT)	1128	33 (97%)
Song *et al.*[34]	26/02/2020	China	Case report	Caesarean section	Throat and faecal RT-PCR, chest CT scan	1	22 (61%)
Sun *et al.*[35]	28/04/2020	China	Case series	Caesarean section	Pharyngeal, laryngeal, throat and tracheal tube tip RT-PCR	3	18 (50%)
Wang *et al.*[36]	28/02/2020	China	Case report	Caesarean section	Throat swab RT-PCR, chest CT scan	1	21 (58%)
Xia *et al.*[37]	17/03/2020	China	Case report	Caesarean section	Oropharyngeal RT-PCR, chest CT-scan	1	14 (38%)
Zeng *et al.*[38]	26/03/2020	China	Case series	Caesarean section	Symptoms, chest CT scan and RT-PCR	6	9 (25%)
Zhang *et al.*[39]	08/04/2020	China	Case series	Caesarean section	Suspected: Abnormal CT scan (ground-glass opacity and	4	17 (47%)

					bilateral patchy shadowing), coupled with typical clinical symptoms (fever, cough, headache, sore throat, shortness of breath), sputum. Confirmed: Nasopharyngeal RT-PCR		
Zhao *et al.*[40]	18/03/2020	China	Clinical study	10 abdominal, 2 cardiovascular , 6 orthopaedic, 11 gynaecology and obstetrics, 2 neurosurgery and 6 other	Laboratory, imaging (CT-scan) and clinical findings (body temperature)	37	10 (29%)
Zhong *et al.*[41]	28/03/2020	China	Case series	45 Caesarean section, 4 orthopaedic	Radiology for inclusion in study, confirmation through throat swab RT-PCR	49	26 (72%)

CARE, CAse REport; CT, computed tomography; RNA, ribonucleic acid; RT-PCR, reverse transcriptase-polymerase chain reaction; STROBE, Strengthening The Reporting of Observational Studies in Epidemiology; UK, United Kingdom; USA, United States of America.

*Details of the STROBE and CARE scores are provided in the methods section

Table 3 – Perioperative management details of patients in the rapid review

Study	Type of Surgery	HCW Use of PPE	HCW Level of PPE	Patient Use of PPE	Patient Level of PPE	Type of anaesthesia	Pain assessment	Analgesics used	Vasopressors used	Bloo
Alzamora *et al*.[16]	1 Caesarean section	Not reported	Not reported	Not reported	Not reported	1 General anaesthesia	Not reported	Not reported	Not reported	N Repo
Catellani *et al*.[17]	13 Orthopaedic	Not reported	Not reported	Not reported	Not reported	13 spinal anaesthesia with nerve block	Not reported	Not reported	Not reported	N repo man w trans
Chehrassan *et al*.[18]	5 Orthopaedic, 1 abdominal	Unclear	Unclear	Unclear	Unclear	Not reported	Not reported	Not reported	Not reported	N repo
Chen *et al*.[19]	17 Caesarean sections	Yes	BSL-3 (N95 masks, goggles, protective suits,	Yes	17 Regular surgical	14 epidural and 3 general anaesthesia	VAS	Epidural anaesthesia - 2% lidocaine,	Not reported	Epi anaes - M

			disposable medical caps, and medical rubber gloves)		masks			0.75% ropivacaine General anaesthesia - 8% sevoflurane, 2% lidocaine, remifentanil, succinylcholine, zsufentanil, propofol		307m 9 Ger anaes – M 300m 10
Doglietto *et al*.[20]	22 Orthopaedic, 7 vascular, 6 neurological, 5 general, 1	Not reported	Not reported	Not reported	Not reported	21 local and 20 general anaesthesia	Not reported	Not reported	Not reported	N repo

	thoracic									
Dong *et al*.[21]	1 Caesarean section	Not reported	Not reported	Yes	N95 mask	Not reported	Not reported	Not reported	Not reported	N repo
Du *et al*.[22]	1 Caesarean section	Yes	Level 3	Yes	N95 mask	Combined spinal and epidural anaesthesia	Not reported	Not reported	Not reported	N repo
Ferrazzi *et al*.[23]	18 Caesarean sections	Yes	More strict PPE than just surgical masks	Yes	18 More strict PPE than just surgical masks	Not reported	Not reported	Not reported	Not reported	N repo
Firstenberg *et al*.[24]	1 Cardiothoracic	Yes	N95 masks with face shield or goggles (in addition to	Not reported	Not reported	General anaesthesia implied from endotracheal	Not reported	Not reported	Not reported	N repo

			surgical gown and gloves)			tubing (but not explicitly stated)				
Gao *et al*.[25]	4 Abdominal	Yes	Full PPE (Level 3)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	N repo
Gidlöf *et al*.[26]	1 Caesarean section	Yes	Not reported	Not reported	Not reported	Spinal anaesthesia	Not reported	Not reported	Not reported	~20
He *et al*.[27]	4 Cardiothoracic	Yes	Level 3	Not reported	Not reported	General anaesthesia	Not reported	Not reported	Not reported	N repo
Lee *et al*.[28]	1 Caesarean section	Yes	N95 mask, surgical cap, double gown, double gloves, shoe covers, powered air-purifying	Yes	N95 mask	Spinal anaesthesia	Not reported	0.5% marcaine, fentanyl (injected intrathecally)	Phenylephrine	40

			respirator							
Li *et al*.[29]	1 Caesarean section	Yes	Protective suit	Yes	Protective suit	Not reported	Not reported	Not reported	Not reported	N repo
Lu *et al*.[30]	1 Caesarean section	Yes	Level 3 (gown, N95 mask, eye protection and three-layer latex gloves)	Not reported	Not reported	Combined spinal and epidural anaesthesia	Not reported	Not reported	Not reported	~20
Lyra *et al*.[31]	1 Caesarean section	Yes	Level 2	Not reported	Not reported	Regional anaesthesia	Not reported	Not reported	Not reported	N repo
Mi *et al*.[32]	Not reported	Not reported	Not reported	Not reported	Not reported	21 Spinal, 3 local and 4 general anaesthesia	Not reported	Not reported	Not reported	N repo
Nepogodiev *et al*.[33]	373 gastrointestinal	Not reported	Not reported	Not reported	Not reported	30-day mortality –	Not reported	Not reported	Not reported	N repo

	and general, 302 orthopaedic, 86 cardiothoracic, 62 hepatobiliary, 51 obstetric, 45 vascular, 40 head and neck, 39 neurosurgery, 37 urological, 57 other and 36 missing					15 local, 32 regional, 217 general anaesthesia; Pulmonary complications - 25 local, 73 regional, 464 general anaesthesia				
Song *et*	1 Caesarean	Unclear	Unclear	Not	Not	Combined	Not	Tramadol	Yes	30

al.[34]	section			reported	reported	spinal and epidural anaesthesia	reported			
Sun *et al.*[35]	3 Caesarean sections	Yes	Full (N95 mask, eye goggles, face shield, top-to-bottom tight-fitting gown)	Yes	1 Not reported, 2 face masks	1 General and 2 spinal anaesthesia	Not reported	Not reported	Not reported	N repo
Wang *et al*.[36]	1 Caesarean section	Yes	Level 3	Not reported	Not reported	Combined spinal and epidural anaesthesia	Not reported	Not reported	Not reported	20
Xia *et al*.[37]	1 Caesarean section	Yes	Third-level measure - N95 mask (fit tested),	Not reported	Not reported	Combined spinal and epidural	Not reported	1% ropivacaine	Intravenous methoxamine	~30

			disposable surgical cap, medical goggles or positive-pressure headgear, disposable protective clothing, disposable gloves, disposable shoe covers			anaesthesia				
Zeng *et al*.[38]	6 Caesarean sections	Yes	Protective suits and double masks	Yes	6 masks	Not reported	Not reported	Not reported	Not reported	N repo

Zhang *et al*.[39]	4 Caesarean sections	Not reported	Not reported	Yes	1 Level 2, 3 level 3	Not reported	Not reported	Not reported	Not reported	N repo
Zhao *et al.*[40]	10 abdominal, 2 cardiovascular , 6 orthopaedic, 11 gynaecology and obstetrics, 2 neurosurgery and 6 other	Unclear (the study states a protocol including level 3 protective measures for operating room staff but not	Not reported	Not reported	Not reported	26 General anaesthesia and 11 spinal anaesthesia	Not reported	Not reported	Not reported	N repo

		specified for which cases PPE was used)								
Zhong *et al*.[41]	45 Caesarean sections, 4 orthopaedic	Yes	37 Level 3 and 7 Level 1	Not reported	Not reported	Spinal anaesthesia	Not reported	2% Lidocaine (2ml) and 0.75% isobaric ropivacaine	Not reported	N repo

BSL, biosafety level; cc, cubic centimeter; HCW, health care worker; ml, millilitre; PPE, personal protective equipment; SD, standard deviation;

Box 1 – The National Health Commission of China's diagnostic criteria for suspected cases of COVID-19 (seventh edition).

A case that has any one condition of epidemiological history and any 2 clinical manifestations is considered as a suspected case. If there is no clear epidemiological history, then suspected cases need all 3 clinical manifestations.

A. Epidemiological history

1. History of residence or travel in Wuhan and its surrounding areas, or in other communities with cases reported within 2 weeks prior to the onset of the disease;
2. History of contact with SARS-CoV-2 infected patients (positive results of nucleic acid test) within 2 weeks prior to the onset of the disease;
3. History of contact with patients with fever and/or respiratory symptoms who are from Wuhan and its surrounding areas, or from other communities with cases reported within 2 weeks prior to the onset of the disease;
4. Cluster of infections: 2 or more cases with fever and/or respiratory symptoms occurred in a small area such as home, office, and school class within 2 weeks prior to the onset of the disease.

B. Clinical manifestations

1. Fever and/or respiratory symptoms;
2. Imaging features of COVID-19: multiple patchy shadows and interstitial changes in the early phase, and then multiple ground-glass opacities, infiltration shadows or even consolidation in advanced-phase;
3. Normal or decreased leucocyte and lymphocyte count in the early stage of disease.

Box 2 – Clinical recommendations for the perioperative management of people with suspected or confirmed COVID-19 and suggestions for further research

A. Clinical Recommendations

During the perioperative period, when COVID-19 is suspected or confirmed:

1. Testing for COVID-19 should be conducted preoperatively. During a pandemic or local outbreak, all patients should be tested.
2. RT-PCR and chest CT scans (along with relevant clinical signs) should be conducted together to confirm COVID-19 diagnosis and reducing waiting times.
3. Surgeries should be conducted in negative pressure operating rooms where possible, with HCWs using Level 3 PPE and patients wearing face masks, if practical, until further evidence is available. During a pandemic or local outbreak all HCWs should use Level 3 PPE for surgeries involving untested patients.
4. Clinicians should consider relevant risk factors of increased mortality in COVID-19 patients including male gender, age >70 years, poor preoperative condition, malignancy and the urgency and extent of surgery before deciding whether to conduct surgery.
5. Strategies should be implemented to reduce the risk of postoperative respiratory complications and associated mortality (e.g. use of regional anaesthesia over general anaesthesia and postponing surgery for patients with correctable pathophysiology).
6. Clinical management should take account of the potential need for prolonged hospital stay, particularly in high risk groups.
7. Clinicians should consider the isolation of neonates immediately after birth if the mother is suspected or confirmed as having COVID-19.

B. Research recommendations

1. Optimal approach to perioperative diagnosing of COVID-19 needs to be determined, taking into account false-negative rate of RT-PCR tests.
2. There should be routine recording and reporting of specific perioperative management approaches, when COVID-19 is suspected or confirmed, including anaesthetics/analgesics used, to allow understanding of their relationships with postoperative outcomes.
3. Individual studies should provide more detailed reporting on the duration of PPE use during the perioperative period, by HCWs and patients, when COVID-19 is suspected or confirmed, and whether any changes should be made for specific procedures (e.g. intubation/extubation).
4. Current and future studies should record and report long term outcomes of surgery in suspected or confirmed COVID-19 for patients and healthcare workers.
5. The length of time following COVID-19 resolution before a patient can undergo surgery, without increased risk, needs to be established.

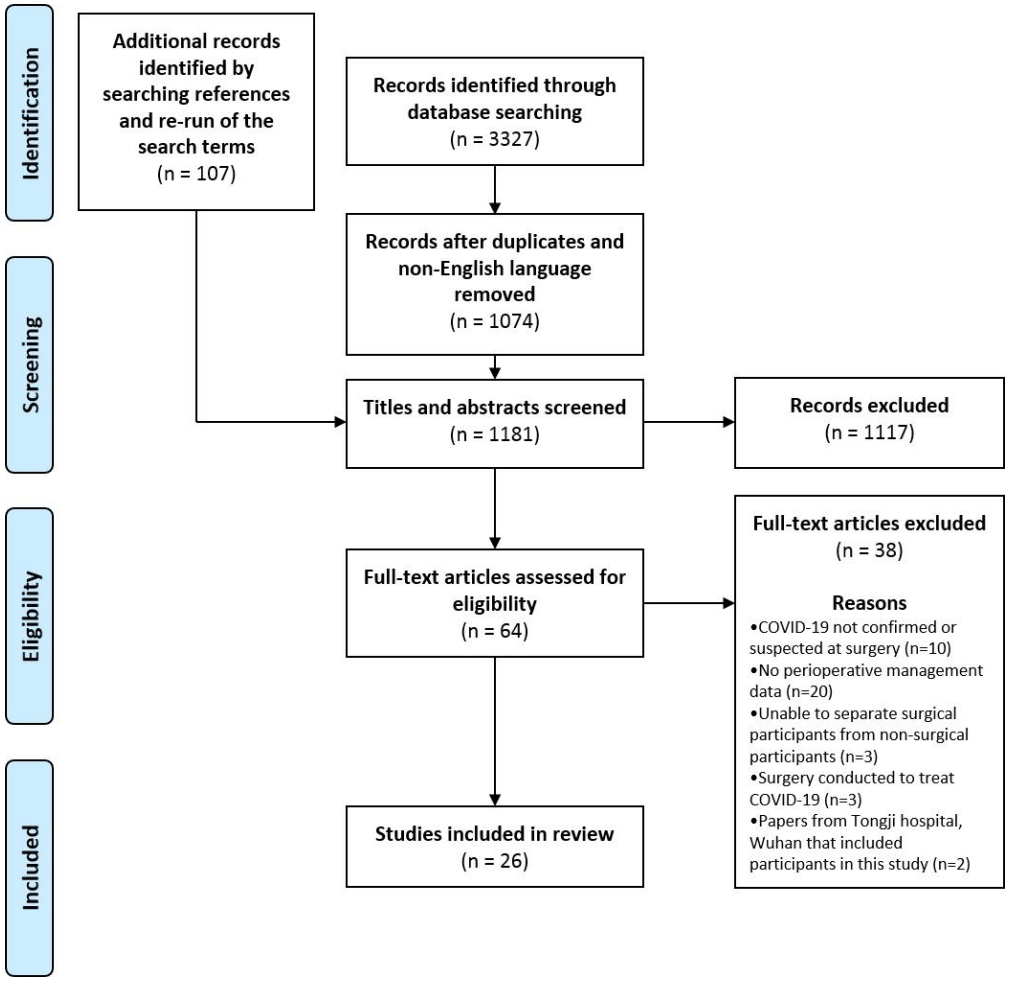

Figure 1. PRISMA flow diagram for the identification and screening of articles for inclusion in the review

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